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# Complete assignments of $^{1}H$ and $^{13}C$ NMR spectral data for 7,7′-dihydroarylnaphthalene lignan lactones

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**In this article we present a complete $^{1}H$ and $^{13}C$ NMR spectral analysis of three 7,7′-dihydroarylnaphthalene lignan lactones using modern NMR techniques such as COSY, HSQC, HMBC and NOE experiments. Complete assignment and homonuclear hydrogen coupling constant measurements were performed.** 

**Keywords:** $^{1}H$ NMR; $^{13}C$ NMR; 2D NMR; apopicropodophyllin; 7,7′-dihydronaphthalene lignan lactone

## Introduction

Lignan lactones are natural products that display several biological properties and have several kinds of chemical skeletons.[1] We have synthesized several natural and synthetic products during our studies on the biological properties of these lignans. The structural elucidation of the obtained compounds furnished important NMR data, which contributed to the completion the spectroscopic data found in the literature for several classes of lignan lactone skeletons.[2–5]

In this article, we describe the spectrometric properties of lignans in which there is a double bond in the C8–C8′ position (Fig. 1). Several lignans containing this type of skeleton were obtained by total and partial synthesis, and we have selected three among these substances to carry out a detailed NMR study. Compounds **1** and **2** were obtained by total synthesis[6] from butenolide 4 (Scheme 1), and $\beta$-apopicropodophyllin (**3**) was prepared from the natural picropodophyllin[7] by partial synthesis (Scheme 2).

Thus, in this article, we present a detailed assignment of the NMR data obtained for such 7,7′-dihydronaphthalene lignan lactones, including the 2D NMR data.

## Experimental

### Materials

Lignans **1** and **2** were prepared from lactone **4**,[7] as described in Scheme 1, whereas lignan **3** was obtained by partial synthesis from picropodophyllin,[7] as shown in Scheme 2.

### NMR measurements

All 1-D ($^{1}H$ and $^{13}C$) NMR experiments were performed on a Bruker Avance DRX400 spectrometer (400.13 MHz for $^{1}H$ and 100.61 MHz for $^{13}C$) equipped with a direct probe head of 5 mm (DUL 13C-1). 2D and nuclear Overhauser effect (NOE) NMR experiments were accomplished on a Bruker Avance DRX500 spectrometer (500.13 MHz for $^{1}H$ and 125.76 MHz for $^{13}C$) equipped with an inverse probe head of 5 mm (BBI 1H-BB). The $^{1}H$ NMR spectra were acquired with an solar water heating (SWH) of 8.28 kHz, TD of 64K, and NS of 16, which provided a digital resolution of *ca* 0.126 Hz ($^{1}H$ 30° pulse width = 8.5 µs). As for the $^{13}C$ NMR spectra, an SWH of 23.98 kHz was employed, with TD of 32K and NS of 1024, giving a digital resolution of *ca* 0.732 Hz ($^{13}C$ 30° pulse width = 14.25 µs). DEPT (512 scans), $^{1}H/^{1}H$ and $^{13}C/^{1}H$ 2D chemical shift correlation experiments were carried out using standard pulse sequences supplied by the spectrometer manufacturer. Long-range $^{13}C/^{1}H$ chemical shift correlations were obtained in experiments with delay values optimized for $^{2}J(C,H) = 8$ Hz. Experiments were performed at 300 K and the concentrations for all samples were in the range 10–15 mg $ml^{-1}$ in $CDCl_3$ or $C_6D_6$, using TMS as internal reference.

## Results and Discussion

In the case of the data initially acquired in $CDCl_3$, the overlap of several resonances precluded the assignment. Therefore, $C_6D_6$ was used as solvent for all samples, which provided much clearer spectra for **2**, but not for **1** and **3**. The $^{1}H$ NMR signals of **2** were resolved by using $C_6D_6$ as solvent, which allowed verification of the multiplicities, observation of the chemical shifts, and measurement of the coupling constants.

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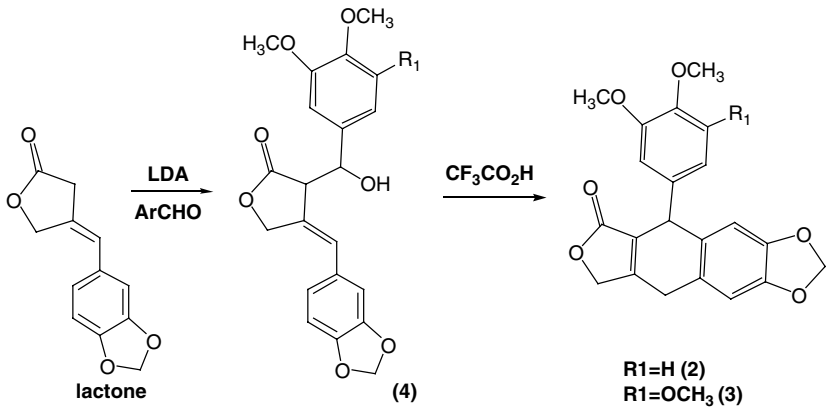
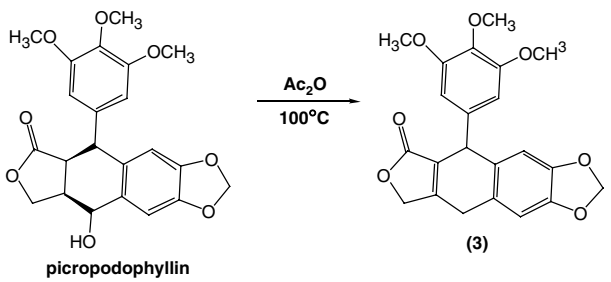
**Table 1.** $^{1}H$ and $^{13}C$ NMR chemical shifts, $\upsilon$ (ppm), multiplicities and coupling constants, $J_{(H-H)}$ (Hz), $^{1}H-^{1}H$ and $^{1}H-^{13}C$ correlations in HMBC, COSY and HMQC spectra for compound **1**

| C | $\delta_C$ (ppm) | H | $\delta_H$ (ppm) | Multiplicity | Coupling constant (Hz) | HMBC | COSY | HSQC |
|---|---|---|---|---|---|---|---|---|
| 1′ | 130.1 | – | – | – | – | – | – | – |
| 2′ | 108.5 | 2′ | 6.52 | br s | – | C-1′,6′,7′ | H-7′,6′ | H-2′ |
| 3′ | 147.8 | – | – | – | – | – | – | – |
| 4′ | 147.3 | – | – | – | – | – | – | – |
| 5′ | 108.3 | 5′ | 6.89 | d | $J_{(5',6')} = 8.2$ | C-6′,1′,7′ | H-6′ | H-5′ |
| 6′ | 121.6 | 6′ | 6.74 | br d | $J_{(6',5')} = 8.2$ | C-5′,1′,2′ | H-5′,7′ | H-6′ |
| 7′ | 42.2 | – | 4.77 | br s | – | C-3,6′,8′,1, 1′,2,8,9 | H-7a,7b,9a, 9b,3,2′ | H-7′ |
| 8′ | 123.4 | – | – | – | – | – | – | – |
| 9′ | 172.1 | – | – | – | – | – | – | – |
| 1 | 128.1 | – | – | – | – | – | – | – |
| 2 | 136.6 | – | – | – | – | – | – | – |
| 3 | 109,4 | 3 | 6.70 | s | – | C-7′ | H-7′,7a,7b, | H-3 |
| 4 | 146.5 | – | – | – | – | – | – | – |
| 5 | 146.9 | – | – | – | – | – | – | – |
| 6 | 107.7 | 6 | 6.60 | s | – | C7,C1,C2 | H-7a,7b, | H-6 |
| 7 | 29.1 | 7a | 3.87 | dd | $J_{(7a,7b)} = 22.3$ $J_{(7a,7')} = 4.1$ | C-3,8′,1,2, 5,8, 9 | H-7′,6,3, 9a,9b,7′,6,3,9a,9b | H-7 |
| | | 7b | 3.65 | dd | $J_{(7b,7a)} = 22.3$ $J_{(7b,7')} = 4.3$ | C-3,8′,1,2, 5,8,9 | | |
| 8 | 157.0 | – | – | – | – | – | – | – |
| 9 | 71.0 | 9a | 4.90 | d | $J_{(9a,9b)} = 17.0$ | C-1,2,8,9 | H-7′,7a,7b | H-9 |
| | | 9b | 4.83 | d | $J_{(9b,9a)} = 17.0$ | | | |
| 10 | 101.3 | 10a | 5.95 | s | – | C-4,5 | H-10b | H-10a |
| | | 10b | 5.92 | s | | | H-10a | H-10b |
| 11 | 100.9 | 11a | 5.90 | s | – | C-3′,4 | H-11b | H-11a |
| | | 11b | 5.83 | s | | | H-11a | H-11b |




**Scheme 1.** Preparation of compounds **1** and **2**.




**Scheme 2.**

Most of the $^{1}H$NMR signals for **1**–**3** are resolved. This allowed us to verify the multiplicities, observe the chemical shifts and measure the coupling constants in most cases. Most $^{13}C$ signals could be assigned through HMQC. For quaternary carbons, comparison with calculated spectra[9] and analysis of HMBC data were sufficient to complete the assignment.

The position of aromatic ring in the C7′ was confirmed by Nuclear Overhauser Effect Difference (NOEDiff) experiments, with irradiation at the frequencies corresponding to H7 and H9. The most important results were the enhancement of the H9 signals when irradiated at the H7 frequency, and the enhancement of

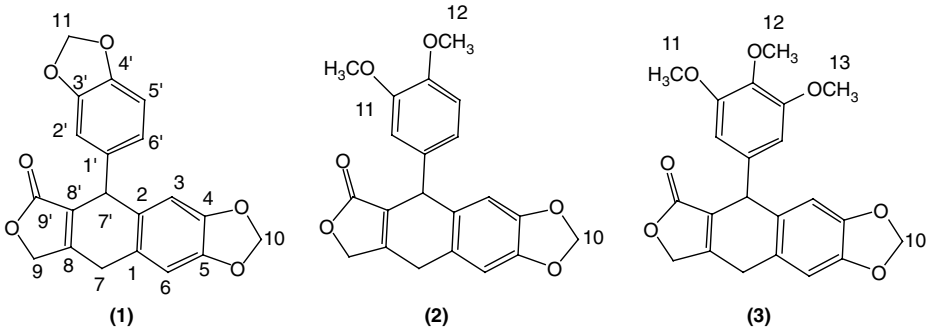



**Figure 1.** Structures of compounds **1**, **2** and **3**.

**Table 2.** $^{1}$H and $^{13}$C NMR chemical shifts, $\upsilon$ (ppm), multiplicities and coupling constants, $J_{(H,H)}$ (Hz), $^{1}$H–$^{1}$H and $^{1}$H–$^{13}$C correlations in HMBC, COSY and HSQC spectra for compound **2**, in $C_6D_6$ for $^{1}$H and in $CDCl_3$ for $^{13}$C NMR

| C | $\delta_C$ (ppm) | H | $\delta_H$ (ppm) | Multiplicity | Coupling constant (Hz) | HMBC | COSY | HMQC |
|---|---|---|---|---|---|---|---|---|
| 1′ | 130.1 | – | – | – | – | – | – | – |
| 2′ | 112.0 | 2′ | 7.00 (1H) | d | $J_{(2',6')} = 2.1$ | C-1′,6′,7′ | H-7 | H-2′ |
| 3′ | 147.8 | – | – | – | – | – | – | – |
| 4′ | 147.3 | – | – | – | – | – | – | – |
| 5′ | 111.2 | 5′ | 6.55 (1H) | d | $J_{(5',6')} = 8.2$ | C-6′,1′,7′ | H-6′ | H-5′ |
| 6′ | 120.2 | 6′ | 6.68 (1H) | dd | $J_{(6',5')} = 8.2$<br>$J_{(6',2')} = 2.1$ | C-5′,1′,2′ | H-5′,7′ | H-6′ |
| 7′ | 42.1 | 7′ | 4.77 (1H) | brs | – | C-3,6′,8′,1,<br>1′,2,8,9 | H-2′,6′ | H-7′ |
| 8′ | 123.7 | – | – | – | – | – | – | – |
| 9′ | 172.3 | – | – | – | – | – | – | – |
| 1 | 128.3 | – | – | – | – | – | – | – |
| 2 | 135.4 | – | – | – | – | – | – | – |
| 3 | 107.7 | 5 | 6.63 (1H) | s | – | C 7′,2 | H-6 | H-3 |
| 4 | 146.7 | – | – | – | – | – | – | – |
| 5 | 146.1 | – | – | – | – | – | – | – |
| 6 | 109.5 | 2 | 6.43 (1H) | s | – | C-7,1,2 | H-3,7,10 | H-6 |
| 7 | 29.2 | 7a | 2.88 (1H) | dd | $J_{(7a,7b)} = 22.3$;<br>$J_{(7a,7')} = 4.3$ | C-3,8′,1,2,5,8,9 | H-9 | H-7 |
| | | 7b | 2.50 (1H) | dd | $J_{(7a,7b)} = 22.3$<br>$J_{(7a,7')} = 4.0$ | C-3,8′,1,2,5,8,9 | | |
| 8 | 157.0 | – | – | – | – | – | – | – |
| 9 | 71.0 | 9a | 3.78 (1H) | d | $J_{(9a,9b)} = 16.8$ | C-1,2,8,9 | H-7 | H-9 |
| | | 9b | 3.73 (1H) | d | $J_{(9b,9a')} = 16.8$ | | | |
| 10 | 101.2 | 10a | 5.33 (1H) | s | – | | H-10b | H-10a |
| | | 10b | | s | | C-4,5 | H-10a | H-10b |
| 11 | 55.8 | 10 | 3.48 (3H) | s | – | C-3′ | – | H-11 |
| 12 | 55.8 | 11 | 3.35 (3H) | s | – | C-4′ | – | H-12 |

the H7 signals when irradiated at the H9 frequency. Results are in agreement with the structures shown in Fig. 1.

The $^{1}$H and $^{13}$C NMR data of compounds **1**, **2** and $\beta$-apopicropodophyllin (**3**) are given in Tables 1, 2 and 3, respectively.

## Conclusion

The assignment of all hydrogen and carbon signals and the measurement of all $^{1}$H/$^{1}$H coupling constants were accomplished for compounds **1**, **2** and **3**. The use of HMQC and COSY allowed determination of most of the chemical shifts and coupling constants. HMBC and spectral simulations solved the more complicated cases. All results were confirmed by spectral simulations.[8] The position of aromatic ring in the C7′ was confirmed by NOEDiff experiments.

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**Table 3.** $^{1}H$ and $^{13}C$ NMR chemical shifts, $\upsilon$ (ppm), multiplicities and coupling constants, $J_{(H,H)}$ (Hz), $^{1}H-^{1}H$ and $^{1}H-^{13}C$ correlations in HMBC, COSY and HMQC spectra for compound **3**, in $CDCl_3$

| C | $\delta_C$ (ppm) | H | $\delta_H$ (ppm) | Multiplicity | Coupling constant (Hz) | HMBC | gCOSY | HMQC |
|---|---|---|---|---|---|---|---|---|
| 1′ | 136.9 | – | – | – | – | – | – | – |
| 2′ | 105.6 | 2′ (1H) | 6.41 | s | – | C-3′,6′,1′,8′ | H-7′ | H-2′ |
| 3′ | 153.1 | – | – | – | – | – | – | – |
| 4′ | 147.2 | – | – | – | – | – | – | – |
| 5′ | 153.2 | – | – | – | – | – | – | – |
| 6′ | 105.7 | 6′ (1H) | 6.41 | s | | C-4′,8′,2′,5′ | H-7′ | H-6′ |
| 7′ | 42.7 | 7′ (1H) | 4.83 | m | – | C-3,6′,2′,8′, | H-3′,6′ | H-7′ |
| 8′ | 128.1 | – | – | – | – | – | – | – |
| 9′ | 172.2 | – | – | – | – | – | – | – |
| 1 | 129.6 | – | – | – | – | – | – | – |
| 2 | 123.7 | – | – | – | – | – | – | – |
| 3 | 109.5 | 3 (1H) | 6.62 | s | – | C-7′,2,1 | H-6 | H-3 |
| 4 | 140.6 | – | – | – | – | – | – | – |
| 5 | 147.0 | – | – | – | – | – | – | – |
| 6 | 107.7 | 6 (1H) | 6.70 | s | – | C-5,1,2,7 | H-3,7,10 | H-6 |
| 7 | 29.2 | 7a (1H) | 3.82 | dd | $J_{7a7b} = 27.9; J_{7a,7'} = 2.5$ | C-2,8′,6 | H-9 | H-7 |
| | | 7b (1H) | 3.64 | dd | $J_{7b7a} = 27.9; J_{7b,7'} = 3.5$ | | | |
| 8 | 157.3 | – | – | – | – | – | – | – |
| 9 | 71.1 | 9a (1H) | 4.87 | m | – | C-8′,1,8,9′ | H-7 | H-9a |
| | | 9b (1H) | 4.82 | m | | | | H-9b |
| 10 | 101.3 | 10a (1H) | 5.93 | d | $J_{10a,10b} = 4.5$ | C-4,5 | H-10b | H-10a |
| | | 10b (1H) | 5.90 | d | $J_{10b,10a} = 4.5$ | | H-10a | H-10b |
| 11 | 56.1 | 11 (3H) | 3.76 | s | – | C-3′ | – | H-11 |
| 12 | 60.7 | 12 (3H) | 3.79 | s | – | C-4′ | – | H-12 |
| 13 | 56.1 | 13 (3H) | 3.76 | s | – | C-5′ | – | H-13 |

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